Citation:

Silvera SA, Jain M, Howe GR, Miller AB, Rohan TE. Dietary carbohydrates and breast cancer risk: A prospective study of the roles of overall glycemic index and glycemic load. *Int J Cancer*. 2005 Apr 20; 114 (4): 653-658. Erratum in: *Int J Cancer*. 2006 May 1; 118 (9): 2,372.

PubMed ID: 15609324

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine breast cancer risk in association with glycemic index (GI), glycemic load (GL), and intake of dietary carbohydrate and sugar.

Inclusion Criteria:

Women aged 40-59 who were enrolled in the Canadian National Breast Screening Study and completed a self-administered food-frequency questionnaire (FFQ) between 1982 and 1985.

Exclusion Criteria:

Extreme energy intake values [at least three standard deviations (SD) above or below the mean value for $\log_e$ caloric intake].

Description of Study Protocol:

Recruitment

Between 1980 and 1985, 89,835 women aged 40-59 years were recruited from the general population into the Canadian National Breast Screening Study (NBSS).

Design

Prospective cohort study.

Dietary Intake/Dietary Assessment Methodology

- Starting in 1982, a self-administered FFQ was distributed, covering 86 food items
- Compared self-administered questionnaire and a full interviewer-administered questionnaire,

the two methods gave estimates of intake of the major macronutrients and dietary fiber that were moderately to strongly correlated (reported correlation coefficients from 0.47 to 0.72).

Blinding Used

Not applicable.

Intervention

Not applicable.

Statistical Analysis

- Cox proportional hazards models (using age as the time scale) were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between energy-adjusted quintile levels of glycemic load, overall glycemic index, total carbohydrates and total sugar, as well as breast cancer risk; energy adjustment was performed using the residual method
- For these analyses, cases contributed person-time to the study from their date of enrollment until the date of diagnosis of their breast cancer, and non-cases contributed person-time from their date of enrollment until the termination of follow-up (the date to which cancer incidence data were available for women in the corresponding province) or death, whichever occurred earlier
- Multivariate models included the variables listed. To test for trend, the median value of each quintile was fitted as an ordinal variable in the risk models and evaluated the statistical significance of the coefficient using the Wald test
- The authors examined the associations overall and within strata defined by menopausal status.

Data Collection Summary:

Timing of Measurements

- FFQ distributed beginning in 1982.
- 16.6-year follow-up.

Dependent Variables

Breast cancer risk.

Independent Variables

- Glycemic load
- Glycemic index
- Total carbohydrate consumption
- Total sugar consumption.

Control Variables

- BMI
- Hormone replacement therapy (HRT)
- Alcohol consumption
- Birth control
- Energy intake
- Physical activity

- Menopausal status
- Fiber intake.

Description of Actual Data Sample:

- *Initial N:* 49,613
- *Attrition (final N):* 49, 111
- *Age:* 40-59 years
- *Ethnicity:* None mentioned
- *Other relevant demographics:* None mentioned
- *Anthropometrics:* None mentioned
- *Location:* Canada.

Summary of Results:

Key Findings

GI, GL, total carbohydrate and total sugar intake were not associated with breast cancer risk in the total cohort. However, there was evidence of effect modification of the association between GI and breast cancer risk by menopausal status (see Table).

Adjusted Hazard Ratios and 95% CIs for the Association Between Overall Glycemic Index and Glycemic Load and Risk of Breast Cancer Stratified by Menopausal Status

	Hazard Ratio (95% CI)		P for interaction
Number of cases per person years	Premenopausal 670-400, 673	Postmenopausal 575/300, 048	
Glycemic load (g per day)			
<125	1.0 (referent)	1.0 (referent)	
125-147	0.95 (0.76-1.18)	1.18 (0.92-1.54)	
148-169	0.81 (0.64-1.02)	1.20 (0.93-1.56)	
>169	0.96 (0.76-1.22)	1.08 (0.82-1.41)	
	P=0.44	P=0.68	0.08
Overall glycemic index			
<63	1.0 (referent)	1.0 (referent)	
64-76	0.95 (0.73-1.23)	1.43 (1.04-1.97)	
77-92	0.77 (0.55-1.06)	1.80 (1.24-2.62)	

>92	0.78 (0.52-1.16)	1.87 (1.18-2.97)	
	P=0.12	P=0.01	P=0.01

Author Conclusion:

Consumption of diets with high GI values may be associated with increased risk of breast cancer among post-menopausal women, possibly more so among subgroups defined by participation in vigorous physical activity, ever use of HRT, and those who are not overweight.

Reviewer Comments:

None.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes

2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	Yes
5.	**Was blinding used to prevent introduction of bias?**	N/A

5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	N/A
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	N/A
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	N/A
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	N/A
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	N/A
7.6.	Were other factors accounted for (measured) that could affect outcomes?	N/A

7.7.	Were the measurements conducted consistently across groups?	N/A
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	N/A
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes